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International Patent Application
No. PCT/DK00/00065
Applicants: SurfArc ApS et al.
Our ref.: P405 PC00

Dear Sirs

With reference to the International Search Report issued on 28 August 2000, an amended set of claims is hereby submitted under Article 19 PCT.

Statement under Article 19(1) (Rule 46.4)

The claims have been amended only with respect to mutual dependency and no amendments have thus been made going beyond the disclosure in the international application as filed.

Yours sincerely,
HØIBERG ApS

Jesper Levin Aamand

Amended claims 1-146 (Replacement sheets 79-95)

c.c. IPEA, (EPO, Munich)

Patent claims

1. Material comprising a substratum, said substratum being contactable with a macromolecule, said material further comprising at least one macromolecule,

said material having a first contact angle a,

said substratum having a second contact angle b_0 when not contacted by a macromolecule, and another second contact angle b_{sat}, when said substratum is saturated by said macromolecules as defined herein,

wherein the relation between said contact angles is as defined by the ratio R,

$$R = (b_0 - a) / (b_0 - b_{sat})$$

and wherein the numerical value of R is in the interval from and including 0 to less than 0.6.

2. Material according to claim 1, said material comprising a substratum, said substratum being contactable with a macromolecule, said material further comprising at least one macromolecule,

said material having a first contact angle a,

said substratum having a second contact angle b_0 when not contacted by a macromolecule,

said contact angle a being substantially identical to said contact angle b_0.

3. Material having a first contact angle and comprising a substratum having a second contact angle, said substratum being contacted by a macromolecule, wherein the relation between said first and second contact angle as defined by the ratio between

i) the difference between said second contact angle, when no macromolecule is present, and said first contact angle, and

ii) the difference between said second contact angle, when no macromolecule is present, and the contact angle of said substratum, when said substratum is saturated by said macromolecules as defined herein,

is more than -0.6 and less than 0.6.

4. Material having a first contact angle and comprising a substratum having a second contact angle, said substratum being contacted by a plurality of soluble substances capable of forming a self-assembled monolayer comprising a macromolecule and having a third contact angle, wherein the relation between said contact angles as defined by the ratio between

i) the difference between the third contact angle of said monolayer, when no macromolecule is present, and said first contact angle, and

ii) the difference between the third contact angle of said monolayer, when no macromolecule is present, and the contact angle of said self-assembled monolayer, when said monolayer is saturated by said macromolecules as defined herein,

is more than -0.6 and less than 0.6.

5. Material according to claim 4, wherein said soluble substance is selected from the group consisting of molecules capable of forming a self-assembled monolayer.

6. Material according to any of claims 1 to 5, wherein said substratum is pretreated or modified.

7. Material according to claim 6 wherein said pretreated or modified substratum is the result of said substratum being contacted by and/or operably linked to a charged group or a hydrophilic compound.

8. Material according to any of the preceding claims, wherein said first contact angle is the advancing contact angle.

9. Material according to claim 8, wherein said first contact angle is in the range of from 50 degrees to 140 degrees.

10. Material according to claim 8, wherein said first contact angle is in the range of from 60 degrees to 125 degrees.

11. Material according to claim 8, wherein said first contact angle is in the range of from 70 degrees to 120 degrees.

12. Material according to claim 8, wherein said first contact angle is in the range of from 75 degrees to 110 degrees.

13. Material according to claim 8, wherein said first contact angle is in the range of from 80 degrees to 100 degrees.

14. Material according to claim 8, wherein said ratio is less than 0.50.

15. Material according to claim 8, wherein said ratio is less than 0.40.

16. Material according to claim 8, wherein said ratio is less than 0.30.

17. Material according to claim 8, wherein said ratio is less than 0.25.

18. Material according to claim 8, wherein said ratio is less than 0.20.

19. Material according to claim 8, wherein said ratio is less than 0.15.

20. Material according to claim 8, wherein said ratio is less than 0.10.

21. Material according to claim 8, wherein said ratio is less than 0.05.

22. Material according to any of claims 1 to 7, wherein said first contact angle is the receding contact angle and wherein said ratio is less than 0.40.

23. Material according to claim 22, wherein said first contact angle is in the range of from 30 degrees to 120 degrees.

24. Material according to claim 22, wherein said first contact angle is in the range of from 40 degrees to 110 degrees.

25. Material according to claim 22, wherein said first contact angle is in the range of from 50 degrees to 100 degrees.

26. Material according to claim 22, wherein said first contact angle is in the range of from 60 degrees to 90 degrees.

27. Material according to claim 22, wherein said first contact angle is in the range of from 70 degrees to 80 degrees.

28. Material according to claim 22, wherein said ratio is less than 0.35.

29. Material according to claim 22, wherein said ratio is less than 0.30.

30. Material according to claim 22, wherein said ratio is less than 0.25.

31. Material according to claim 22, wherein said ratio is less than 0.20.

32. Material according to claim 22, wherein said ratio is less than 0.15.

33. Material according to claim 22, wherein said ratio is less than 0.10.

34. Material according to claim 22, wherein said ratio is less than 0.05.

35. Material according to any of the preceding claims, wherein said material, when contacted by a first determinant comprising a compound selected from the group consisting of a polypeptide, or part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof, is capable of maintaining said compound in a biologically active form.

36. Material according to claim 35 wherein said compound is a polypeptide or part thereof.

37. Material according to claim 35 or 36 further comprising said first determinant comprising said compound, wherein said first determinant is maintained in a biologically active form when contacted by said substratum and/or said macromolecule.

38. Material according to claim 37 wherein said biologically active form is essentially a biologically active conformation.

39. Material according to any of claims 35 to 38 wherein said biologically active form or conformation is maintained and/or improved and/or stabilized by means of the cooperativity of said substratum and said macromolecule.

40. Material according to claim 35 to 39 wherein said biologically active form or confirmation is maintained and/or improved and/or stabilized when contacted by said substratum and said macromolecule.

41. Material according to any of the preceding claims, wherein said material is biocompatible.

42. Material according to any of the preceding claims, wherein the weight increase per area unit arising from the part of the macromolecule essentially consisting of PEG or poly(ethylene oxide) (PEO) is less than 2.0×10^{-22} grams (g) per square nanometer (nm^2).

43. Material according to claim 42, wherein said difference is less than 1.0×10^{-22} grams (g) per square nanometer (nm^2).

44. Material according to claim 42, wherein said difference is less than 0.8×10^{-22} grams (g) per square nanometer (nm^2).

45. Material according to claim 42, wherein said difference is less than 0.5×10^{-22} grams (g) per square nanometer (nm^2).

46. Material according to claim 42, wherein said difference is less than 0.3×10^{-22} grams (g) per square nanometer (nm^2).

47. Material according to any of the preceding claims, wherein said substratum is contacted by a plurality of soluble compounds capable of forming a layer of self-assembled macromolecules.

48. Material according to claim 47, wherein said soluble compounds are n-alkane chains preferably containing from 8 to 24 carbons.

49. Material according to any of the preceding claims wherein each macromolecule is associated with an excluded volume.

50. Material according to any of the preceding claims, wherein said substratum comprises a hydrophobic polymer.

51. Material according to claim 50, wherein said substratum is at least substantially flexible.

52. Material according to claim 50, wherein said substratum is a film.

53. Material according to claim 50, wherein said substratum is essentially rigid or at least substantially non-flexible.

54. Material according to claim 53, wherein said substratum comprises a crystalline structure capable of supporting a self-assembled monolayer such as gold, silicon oxide, and similar crystalline structures and/or structures that are smooth on a nanometer scale.

55. Material according to any of the preceding claims, wherein said macromolecule comprises a hydrophilic polymer.

56. Material according to claim 55, wherein said macromolecule comprises an amphiphilic polymer.

57. Material according to any of the preceding claims, wherein said macromolecule has a MW of more than 400 Da.

58. Material according to claim 57, wherein said macromolecule has a MW of more than 1.000 Da.

59. Material according to claim 57, wherein said macromolecule has a MW of more than 5.000 Da.

60. Material according to claim 57, wherein said macromolecule has a MW of more than 10.000 Da.

61. Material according to claim 57, wherein said macromolecule has a MW of more than 50.000 Da.

62. Material according to claim 57, wherein said macromolecule has a MW of more than 100.000 Da.

63. Material according to any of the preceding claims, wherein said macromolecule is a conjugate comprising a head group, a guiding group, a linker group, a polymer chain or a main body, and a functional end group.

64. Material according to claim 63, wherein said head group is capable of forming a chemical bond.

65. Material according to claim 63, wherein said head group may adsorb to the substratum.

66. Material according to claim 63, wherein said head group is capable of forming an ionic bond.

67. Material according to claim 63, wherein said head group may be entangled into or with the substratum.

68. Material according to claim 63, wherein said head group is capable of forming a self-assembled monolayer.

69. Material according to claim 63, wherein said guiding group is a bifunctional group comprising an aliphatic, linear or weakly branched group.

70. Material according to claim 63, wherein said linker group is capable of being enzymatically or chemically hydrolyzed.

71. Material according to claim 63, wherein said linker group is hydrolytically unstable.

72. Material according to claim 63, wherein said linker group is essentially stable against cleavage under practical circumstances.

73. Material according to claim 63, wherein said polymer chain or main body is preferably hydrophilic, uncoiling in an aqueous environment and exhibiting an excluded volume.

74. Material according to claim 63, wherein said functional end group is capable of linking permanently or reversibly other biological or synthetic molecules or materials.

75. Material according to any of claims 35 to 74, wherein said first determinant comprises a biologically active compound comprising a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

76. Material according to claim 75, wherein said biologically active compound comprises a polypeptide.

77. Material according to claim 75, wherein said biologically active compound is selected from the group consisting of membrane associated and/or extracellular matrix polypeptides natively produced by a microbial cell, a plant cell or a mammalian cell.

78. Material according to claim 75 wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

79. Material according to claim 75, wherein said biologically active compound is a synthetic polypeptide, or part thereof, capable of contacting said substratum and/or said macromolecule.

80. Material according to claim 75, wherein said biologically active compound is a synthetic polypeptide, or part thereof, capable of contacting said substratum and said macromolecule.

81. Material according to claim 75, wherein said biologically active compound is an adhesion polypeptide, preferably fibronectin or vitronectin.

82. Material according to any of claims 35 to 81, wherein said biologically active compound results in an improved contact between said material and a biological entity, such as a biological cell or a virus, or part thereof, including a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

83. Material according to any of the preceding claims, said material further comprising a second determinant.

84. Material according to claim 83, wherein said second determinant comprises a biological entity, such as a biological cell or a virus, or part thereof, including a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

85. Material according to claim 83, wherein said biological entity is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a

monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a differentiation factor, a growth factor, and an antagonist to the receptor.

86. Material according to claim 84, wherein said biological cell, or part thereof, is selected from the group consisting of a mammalian cell, including a human cell and an animal cell, a plant cell, a microbial cell, including a eukaryotic microbial cell, including a yeast and a fungus, and a prokaryotic microbial cell including a bacteria.

87. Material according to claim 86 wherein said biological cell is a mammalian cell.

88. Material according to claim 84, wherein said virus, or part thereof, is selected from a mammalian virus, including a human virus and an animal virus, a plant virus, a microbial virus, including a eukaryotic microbial virus, including a yeast virus and a fungal virus, and a prokaryotic microbial virus including a bacteriophage.

89. Material according to claim 88 wherein said virus is a mammalian virus.

90. Material according to any of the preceding claims, wherein said substratum is porous and preferably a membrane.

91. Material according to claim 90, wherein the flux of water through said material is substantially unchanged as compared to the flux of water through said porous substratum.

92. Material according to any of claims 1 to 91, wherein said substratum is non-porous and/or substantially non-penetrable to water.

93. Material according to any of the preceding claims for use in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo.

94. Material according to any of the preceding claims for use in a method of separating and/or isolating biological material ex vivo.

95. Material according to any of the preceding claims for use in a method of producing a biohybrid organ ex vivo.

96. Material according to any of claims 1 to 95 for use in a diagnostic method carried out on the human or animal body.

97. Material according to any of claims 1 to 96 for use in a method of therapy carried out on the human or animal body.

98. Material according to any of claims 1 to 97 for use in a method of surgery carried out on the human or animal body.

99. Material according to any of claims 1 to 98 for use in a method of producing a biohybrid organ in vivo.

100. Material according to any of claims 1 to 99 for use as a carrier for in vivo delivery of a medicament to a human or animal body in need of said medicament.

101. Material according to any of claims 1 to 100 for use in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation in vivo.

102. Material according to any of claims 1 to 101 for use in a method of separating and/or isolating biological material in vivo.

103. Composition comprising the material according to any of the preceding claims and a physiologically acceptable carrier.

104. Pharmaceutical composition comprising the material according to any of claims 1 to 102 or the composition of claim 103 and a pharmaceutically active ingredient and optionally a pharmaceutically active carrier.

105. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of therapy carried out on the human or animal body.

106. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of surgery carried out on the human or animal body.

107. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a diagnostic method carried out on the human or animal body.

108. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of producing a biohybrid organ in vivo.

109. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 as a carrier for in vivo delivery of a medicament to a human or animal body in need of said medicament.

110. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation in vivo.

111. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of separating and/or isolating biological material in vivo.

112. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo.

113. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of separating and/or isolating biological material ex vivo.

114. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in a method of producing a biohybrid organ ex vivo.

115. Use of the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 in the manufacture of an implantable organ or part thereof.

116. Use of the material according to any of claims 1 to 102 as a carrier for a pharmaceutically active ingredient or a pharmaceutical composition.

117. Method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation ex vivo, said method comprising the steps of contacting a cell with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said cell and said material under conditions allowing said cell to grow and/or proliferate and/or differentiate.

118. Method of separating and/or isolating biological material ex vivo, said method comprising the steps of contacting said biological material to be separated and/or isolated with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said biological material and said material under conditions that allow separation and/or isolation.

119. Method of producing a biohybrid organ ex vivo, said method comprising the steps of contacting biohybrid organ cells with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said biohybrid organ cells under conditions allowing the production of said biohybrid organ.

120. Method of therapy carried out on the human or animal body, said method comprising the step of contacting said body with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104.

121. Method of surgery carried out on the human or animal body, said method comprising the step of contacting said body with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104.

122. Method of diagnosis carried out on the human or animal body, said method comprising the steps of contacting said body with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and detecting a signal generated directly or indirectly by said material.

123. Method of controlling cellular growth and/or cellular proliferation and/or cellular differentiation in vivo, said method comprising the steps of contacting a cell with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said cell and said material under conditions allowing said cell to grow and/or proliferate and/or differentiate.

124. Method of separating and/or isolating biological material in vivo, said method comprising the steps of contacting said biological material to be separated and/or isolated with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said biological material and said material under conditions that allow separation and/or isolation.

125. Method of producing a biohybrid organ in vivo, said method comprising the steps of contacting biohybrid organ cells with the material according to any of claims 1 to 102 or the composition according to claim 103 or the pharmaceutical composition according to claim 104 and incubating said biohybrid organ cells under conditions allowing the production of said biohybrid organ.

126. Method of in vivo delivery of a medicament to a human or animal body in need of said medicament, said method comprising the steps of contacting said body with the pharmaceutical composition according to claim 104 and incubating said body contacted by said pharmaceutical composition under conditions allowing delivery of said medicament.

127. Method for producing the material according to any of claims 1 to 102, said method comprising the steps of i) providing a substratum having a second contact angle, and ii) contacting said substratum with a composition comprising a plurality of macromolecules.

128. Method according to claim 127, wherein said substratum comprises a hydrophobic polymer.

129. Method according to claim 127, wherein said substratum is pretreated prior to being contacted by said macromolecule.

130. Method according to claim 129, wherein said pretreatment is effective in increasing the wettability of said substratum.

131. Method according to claim 127, wherein said macromolecule comprises a hydrophilic polymer.

132. Method according to claim 127, wherein said macromolecule comprises a latently reactive polymer.

133. Method according to claim 127, wherein macromolecule has a MW of more than 400 Da.

134. Method according to claim 127, wherein said macromolecule comprises a conjugate comprising a cross likable head group, a linker group, a polymer chain, and a functional end group.

135. Method according to claim 134, wherein said cross likable head group is a photo-reactive aryl azide head group.

136. Method according to claim 134, wherein said macromolecule further comprises a modifying agent.

137. Method according to claim 136 wherein said modifying agent is capable of contacting said substratum and forming a self assembled monolayer.

138. Method according to any of claims 127 to 137 for producing the material according to any of claims 1 to 102, said method comprising the further step of contacting said material with a first determinant comprising a biologically active compound.

139. Method according to claim 138, wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

140. Method according to claim 138, wherein said biologically active compound is a membrane associated and/or extracellular matrix polypeptide natively produced by a microbial cell, a plant cell or a mammalian cell.

141. Method according to any of claims 138 to 140 for producing the material according to any of claims 1 to 102, said method comprising the further step of contacting said material with a second determinant comprising a biological entity.

142. Method according to claim 141, wherein said biological entity comprises a cell or a virus, or a part thereof.

143. Method according to claim 142, wherein said cell, or part thereof, is selected from the group consisting of a mammalian cell, including a human cell and an

animal cell, a plant cell, a microbial cell, including a eukaryotic microbial cell, including a yeast and a fungus, and a prokaryotic microbial cell including a bacteria.

144. Method according to claim 142, wherein said virus, or part thereof, is selected from a mammalian virus, including a human virus and an animal virus, a plant virus, a microbial virus, including a eukaryotic microbial virus, including a yeast virus and a fungal virus, and a prokaryotic microbial virus including a bacteriophage.

145. Method according to claim 141, wherein said biological entity comprises a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof.

146. Method according to claim 141, wherein said biological entity is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a differentiation factor, a growth factor, and an antagonist to the receptor.